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Exploring Meaningful Patient Engagement in ADAPTABLE (Aspirin Dosing: A Patient-centric Trial Assessing Benefits and Long-term Effectiveness)

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Background: Genuine patient engagement can improve research relevance, impact and is required for studies using the National Patient-Centered Clinical Research Network including major multicenter research projects. It is unclear, however, how best to integrate patients into governance of such projects.

Methods: ADAPTABLE (Aspirin Dosing: A Patient-centric Trial Assessing Benefits and Long-term Effectiveness) is the first major multicenter research project to be conducted in National Patient-Centered Clinical Research Network. Here, we provide a description of how we implemented patient engagement in ADAPTABLE thus far, including a description of committee structures and composition, first-hand patient testimonials, specific contributions, and lessons learned during the planning and early implementation of ADAPTABLE.

Results: We recruited 1 patient leader from 6 of the 7 enrolling networks to serve on a Patient Review Board for ADAPTABLE, supported the Board with an experienced patient engagement team including an "investigator-advocate" not otherwise involved in the trial, and facilitated bidirectional communication between the Board and ADAPTABLE Coordinating Center. The Board has reviewed and provided substantial input on the informed consent procedure, recruitment materials, patient portal design, and study policy including compensation of participants. Although it was "too late" for some suggested modifications, most modifications suggested by the patient leaders have been implemented, and they are enthusiastic about the study and their role. The patient leaders also attend Steering and Executive Committee calls; these experiences have been somewhat less productive.

Conclusions: With adequate support, a cadre of committed patient leaders can provide substantial value to design and implementation of a major multicenter clinical trial.

Key Words: patient-centered Review Board, patient engagement, ADAPTABLE, Adaptors

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Engaging patients as stakeholders in patient-centered comparative effectiveness research is essential to answer questions in research that are important to patients and caregivers.[1–4] The Patient-Centered Outcomes Research Institute (PCORI) has transformed the clinical research landscape by its institutional commitment to funding only research projects with genuine patient and stakeholder engagement.[5] As a flagship PCORI project, the National Patient-Centered Clinical Research Network (PCORnet) is designed to leverage major patient partnerships and engage patients meaningfully in all PCORnet research.

It is unclear, however, how patients will engage with major multicenter research projects that PCORnet will enable. The PCORI Methodology Report defines patient engagement including defining research topics and formulating study questions; identifying a study population and choosing interventions, comparators and outcomes; developing optimal strategies for recruitment and retention of study participants; conducting a study and analyzing results; and disseminating research findings into clinical practice.[6] Although, these activities are all relevant to major multicenter research projects, the governance for these projects is already quite complex, typically including a coordinating center, multiple clinical sites, a Steering Committee (SC), an Executive Committee (EC), a data and safety monitoring board, contractors, and often a sponsor oversight body. How patients will fit into this governance structure, interact with professional researchers and clinicians, and contribute meaningfully in this context are open questions.

ADAPTABLE (Aspirin Dosing: A Patient-centric Trial Assessing Benefits and Long-term Effectiveness) is a multicenter pragmatic randomized controlled trial designed to compare the effectiveness of 2 once-daily doses of aspirin for secondary prevention in patients with atherosclerotic cardiovascular disease.[4] ADAPTABLE will recruit 20,000 patients at high risk for ischemic events, randomize them (1:1) to receive an aspirin dose of

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81 mg/d versus 325 mg/d, and follow them for cardiovascular and bleeding events over the course of 3 years.

Patient engagement has been carefully planned and implemented throughout the trial, including constitution of a Patient Review Board for the study comprised of "Adaptors," the patient leaders engaged to help lead ADAPTABLE. Here, we provide a description of how we have implemented patient engagement in ADAPTABLE thus far, including a description of committee structures and composition, first-hand Adaptor testimonials, specific contributions of the Adaptors, and lessons learned during the planning phases and early implementation of ADAPTABLE.

METHODS

The Adaptors: A Patient Review Board for ADAPTABLE Supported by the Health eHeart Alliance

The Adaptors were envisioned as patient leaders who would comprise a Patient Review Board for ADAPTABLE tasked with watching over the study and ensuring that it remained "patient centered." Specifically, the Adaptors would have roles in study planning, review of patient-facing materials, recruitment support, and dissemination of study updates and final results. By design, one Adaptor would be identified from each of the 7 participating PCORnet Clinical Data Research Networks (CDRNs) in order to represent patient viewpoints from the geographic region of the participating sites and to facilitate bidirectional communication between each network, the Coordinating Center and SC. Adaptors are patients that fit most, if not all, of the inclusion /exclusion criteria for the study and are identified by a study site; we have 3 female and 3 male Adaptors. One CDRN is still actively looking for a patient leader. Each Adaptor would participate as a member of the SC and also as a member of the Patient Review Board, which would be hosted and supported by the Health eHeart Alliance, a PCORnet Patient-Powered Research Network focused on cardiovascular health.[7] Support for each Adaptor was budgeted through the Health eHeart Alliance, which contracts with Adaptors as consultants and supports travel and convening for trial activities.

An Interim Description of Process and Outcomes

With news of conditional approval by the PCORI Board of Governors for ADAPTABLE in May 2015, the Duke Clinical Research Institute (DCRI, lead institution for the ADAPTABLE Coordinating Center) and the Health eHeart Alliance initiated recruitment, orientation and engagement of the Adaptors identified from each participating CDRN. After one-on-one training and onboarding calls were completed, official Adaptor activities commenced on September 8, 2015 and are ongoing. The Results below describe process and outcomes, organized by Adaptor activity, through enrollment of the first ADAPTABLE participant on April 19, 2016.

RESULTS

The Adaptor Patient Review Board Conference Calls

The Adaptor Patient Review Board is comprised of the Adaptors, Health eHeart Alliance leadership, and a liaison from the Coordinating Center at DCRI. The Board convenes every other week via conference call, hosted by the Health eHeart Alliance, to discuss and provide input on study operations. The Adaptors have found these calls to be engaging and productive (Table 1, quotes 1–3). Below we describe some of the process features of these conference calls.

Calls are facilitated by an experienced patient engagement team that includes the Project Director and the Principal

TABLE 1. Testimonials to Adaptor Engagement

#	Quoted Testimonial	Role of Quoted Individual (N = 6)
1	"The teamwork is what made this special and so unique. This is not how this [research] has been done in the past. We are patients across the country—on the line with doctors contributing, getting to collaborate and feel the teamwork. We would negotiate and come together—different people have different thoughts and when you put it all together it is special"	Adaptor
2	"The value of this for patients is immense—but when PATIENTS are saying this, this carries a different kind of respect. This is respect that comes from the patient community. … the patients do not fully understand the outcomes yet, but in a few years we will see them". In a few years we can step back and one day we will say "WOW this work was worth it!"	Adaptor
3	"Just [all of] us working together! Sometimes something would come to my mind (and as a patient you worry is this right or wrong) but then another Adaptor will speak up—and we worked together for changes (even if they are small) and overall we did some good work"	Adaptor
4	"... the [value] feels like it is getting lost in other calls, like the SC calls. There is a bit of an arrogance when actually engaging the ADAPTORS. Need to be leveraging the PCORI message more to help bring people into the network"	Adaptor
5	"This is the most exciting and interesting work I have ever done in multicenter trials—thanks to the Adaptors, we see patients as our research partners not simply participants. We are learning together as we go forward and implementing many of these ideas in other new trials"	DCRI Coordinating Center representative
6	"While many around the country are talking about patient engagement in clinical trials, the ADAPTORS have been truly involved in every aspect of the trial including study design, early implementation, and study guidance at the Steering Committee level. While this has not been a smooth process (at times), I suspect that this will be a model utilized many times in the future"	ADAPTABLE investigator

ADAPTABLE indicates Aspirin Dosing: A Patient-centric Trial Assessing Benefits and Long-term Effectiveness; DCRI, Duke Clinical Research Institute; PCORI, Patient-Centered Outcomes Research Institute.

Investigator of the Health eHeart Alliance. The Project Director provides a single point of contact for the Adaptors, and a conduit of information from the Coordinating Center, queues up items for discussion on the agendas, reports Adaptor feedback back the Coordinating Center, and serves as a bridge for the CDRN engagement teams. The Principal Investigator, who is an experienced investigator, not otherwise involved in ADAPTABLE, acts as an investigator-advocate for the Adaptors and an unconflicted "translator" between the patient and researcher perspectives.

We use a round-robin discussion format during each call. Calls always start with "Check-Ins" where each participant says what is on their mind as they settle into the call, and end with "Check-Outs" where we capture any final comments, questions, or concerns for discussion on the next call. In addition, when discussing specific issues, we try to repeat this round-robin format to give each Adaptor an explicit chance to provide input. An example of agenda topics may include: reviewing PHI breach protocol, discussing newsletter topics or reviewing CDRN recruitment materials. Although these processes take time, they appear to be critical for building trust and eliciting input.

The Adaptor Board does not use any video or web conference software, and instead uses Google Docs as a shared display and workspace during conference calls. The online document, upon which the agenda is displayed and notes are taken in real time (by all participants simultaneously, though primarily by Alliance staff), provides running documentation of discussions and decisions made by the Adaptors. The notes are used by the Coordinating Center (the link is stable over time) and distributed to CDRNs and contractors as needed. This method appears to provide visual support for the discussion with minimal technology overhead for our Adaptors, while also facilitating transparent communications with the Coordinating Center.

SC and EC Participation

Along with participating on the Adaptor Patient Review Board, all Adaptors are official members of the ADAPTABLE SC and 2 Adaptors were elected to serve on the EC. The SC group, comprised of the Adaptors, 3 investigators from the Coordinating Center, 1-2 clinical investigators from participating CDRNs, and 3 external advisors, has met by conference call every other week through study startup. The EC has convened once, mid-April with the patient leads, and will continue to meet quarterly.

Although the Adaptors are welcomed and invited to speak in this forum, they have felt less engaged. This is partly due to the size of the SC, a meeting schedule that was not always conducive of consistent Adaptor attendance, and the topics were often of a clinical nature. Adaptors attending those meetings, however, have also felt that their presence is less valued in this forum (Table 1, quote 4), and they do not speak up as frequently as in the Adaptor Board calls.

Adaptor Contributions to Study Policy and Materials

Through their participation on the Adaptors Patient Review Board and the SC, the Adaptors have been asked to review various aspects of study policy and a variety of specific patient-facing study materials. They have contributed both reactively as well as proactively, providing many specific suggestions and also new unsolicited ideas about how to approach and engage participants, via close review of ongoing Adaptor meeting notes we were able to create Table 2, which provides a partial listing of contributions to study policy and materials. We continuously follow-up with the Coordinating Center to assess if and how Adaptor feedback was utilized and report back to our patient leaders; the majority of Adaptor suggestions have been implemented by the Coordinating Center, though some major suggestions have not (eg, celebrity videos and some of the functionality of the portal, Table 2). Anecdotal testimonials to Adaptor engagement utility from Coordinating Center staff and investigators have been overwhelmingly positive (Table 1, quotes 5-6). The Adaptors are now engaging with the ADAPTABLE communications team to codesign a website for the Adaptors that will describe their activities and communicate how ADAPTABLE is engaging patients "differently," with the goal of inspiring positive participation in ADAPTABLE from patients across the country.

DISCUSSION

The Adaptors provide an example of successful integration of patients into governance of a major multicenter PCORnet research project. Although not all of their early interactions with the study have been positive, they remain inspired and productive, and have provided valuable contributions especially to patient-relevant policy and patient-facing study materials.

A number of lessons are evident from our experiences to date. First, it is clear that patients can be most productive when they are supported with dedicated sessions that can be designed for positive patient engagement. In our experience, the large SC conference calls were not ideal in this regard and did not yet yield substantial contributions from patients. For future calls we suggest making sure there are agenda items included that are patient focused as well as reminders made to the leader of the call to actively include the patient participants. In contrast, dedicated regular sessions designed for patients appeared to be highly successful. The key features of these dedicated sessions were: (1) provision of a supportive forum for discussion and fostering an atmosphere of mutual respect and self-efficacy; (2) building the Adaptors' research knowledge base and keeping them informed of the trial progress; and (3) bringing and framing relevant issues to the group, eliciting Adaptor feedback, and delivering that feedback back to the ADAPTABLE leadership team.

Second, it is best to start early with engagement and provide opportunities for patients to have input at the formative stage of study development. Several of the major new ideas brought forward by the Adaptors were not implemented because it appeared to be "too late" to do so. Although this may be somewhat inevitable, we believe earlier engagement would have ameliorated the issue and on subsequent projects we are recommending that identification of a patient representative be included as a contracted milestone.

TABLE 2. Actionable Adaptor Feedback

Category of Input		Specific Modifications Proposed	Implemented (Y/N)	Comments
Review study materials	Informed consent	Change the name of comprehension questions from "quiz" to "review"	Y	Participated in cognitive interview process along with other patients to help shape the development of the consent form
		Shortening the consent review: combine 4 questions into 2, drop 2 questions	Y	Patients felt there was some redundancy in the original 4 questions and we were able to shorten the review to 2 questions
	Recruitment letters	Language changes: specifically, shorter and simpler	Y	
	Other recruitment materials: (flyers, emails)	Language changes, background color for screens as well as, clearly pointing to location of study webpage	Y	
	Patient portal	Language changes on: thank you page, study description, profile	Y	
		Change welcome picture "Everyone looks unhappy…"	Y	
		Portal color scheme—dark blue is easier to read	Y	
		Add functionality allowing participants to leave portal and return later to the same place in the consenting process on the webpage	N	Not able to save information or location before consent
		Add phone number, email, or code to follow-up with patients who leave portal before consent: specifically, "can we find out why they did not make it all the way through?"	N	Not able to collect information for follow-up before consent
		The appropriate time/ place to collect SSN: "after onboarding, only last 4, make it optional"	Y	Adaptors gave study team confidence to collect this piece of information!
		Increase font size	Y	Adjusted length of document in order to increase font size
	Onboarding process	Streamlined questions during onboarding	Y	
		No: 0,1, O, L, or I's in the "golden ticket" number for portal entry	Y	
		Onboarding too long	Y	Removed medication modules to a subsequent visit to shorten the onboarding/ randomization process
Study policies	Compensation	Allow participants to opt out of $25 compensation "donate to research" option	Y	Can opt out, but not able to donate $25 elsewhere
	Trial publicity	Language on the portal describing Adaptors	Y	
		Promotional videos with celebrities, musicians, well known community members	N	Funding was limited and felt best to spend in other areas
		PSA highlighting Adaptable to larger community	Y	American Heart Association (AHA) will be distributing patient-directed PSA in the local CDRN communities
		Adaptors page dedicated to the patient leaders	Y	In progress
		Link from trial webpage to the Health eHeart Alliance forum for broad community engagement	TBD	

CDRN indicates Clinical Data Research Networks; N, no; PSA, Public Service Announcement; TBD, to be determined; Y, yes.

Third, we believe the Adaptors have benefited from having a "critical mass" of patients. As implied by some of the quoted testimony, the Adaptors encourage each other, and take strength from shared discussions and coformulated ideas. Employing a single patient partner/leader or even 2-3 patients may not be likely to produce the same type of shared strength and focus group type dynamic that has proven to be effective in this group.

In any case, ADAPTABLE is now launched, and the Adaptors now enter a different phase of participation. Our role in patient engagement will expand now to include designing and disseminating study updates that we will send to the study participants and also, we hope, to the broader patient community. It will be our goal to design a study update format that will be patient friendly, engaging, and help support the ongoing participation of patients over the 3 years of the trial. The Health eHeart Alliance plans to leverage its own patient community as well as its community forum to encourage dissemination of the updates and conversation about the trial in general. How best to design and support these study updates, and how frequently we should produce them has yet to be decided, but we are comforted by the knowledge that we are working side-by-side in this endeavor with a set of extraordinary and generous patient leaders who are truly engaged and committed to the project.

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